Optimal DAPT Duration for PCI Patients at High Beeding Risk

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Disclosure

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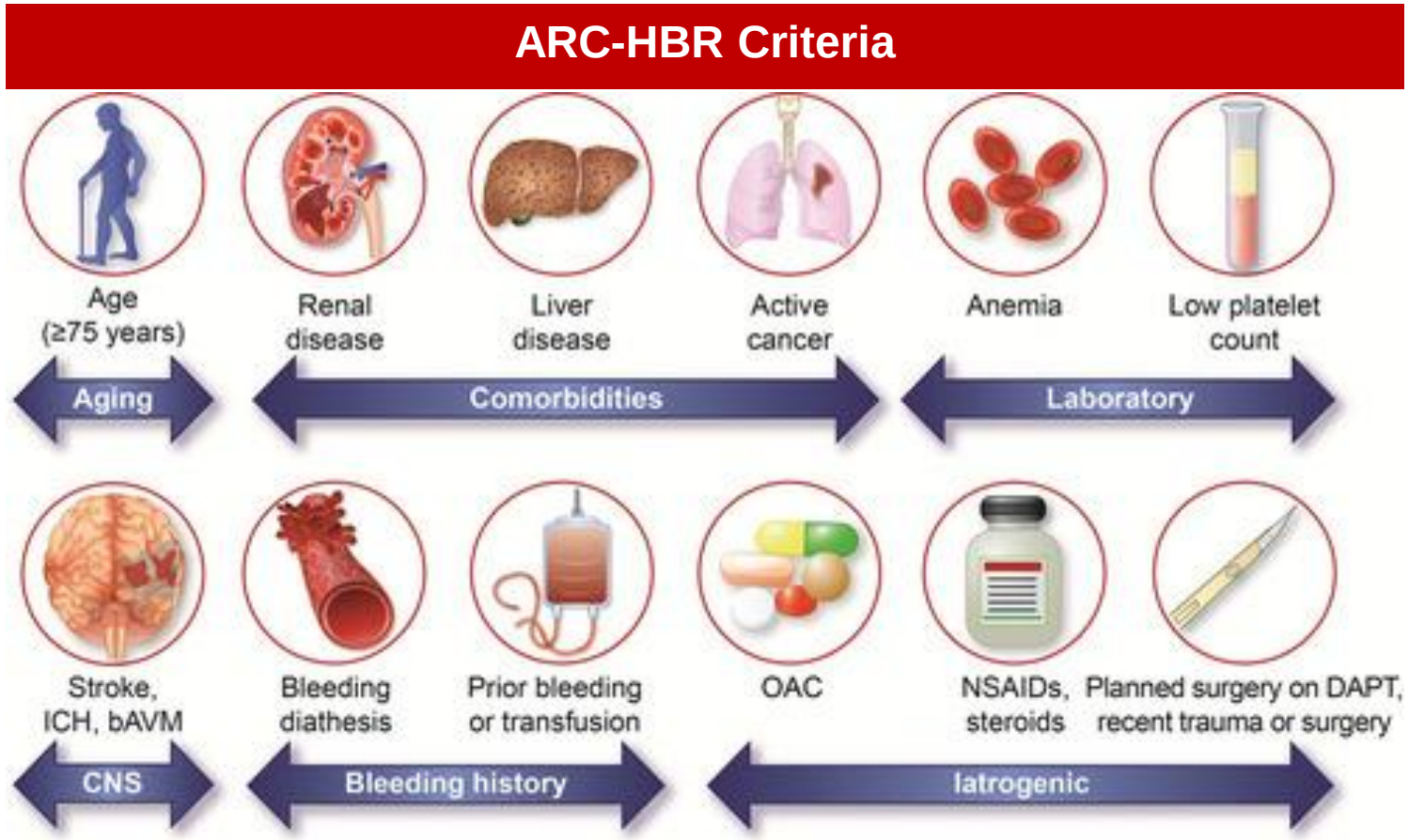
Equity, <1%	Applied Therapeutics, Elixir Medical, STEL, ControlRad (spouse)
Scientific Advisory Boards/Committees	AMA, ACC (BOT member), SCAI

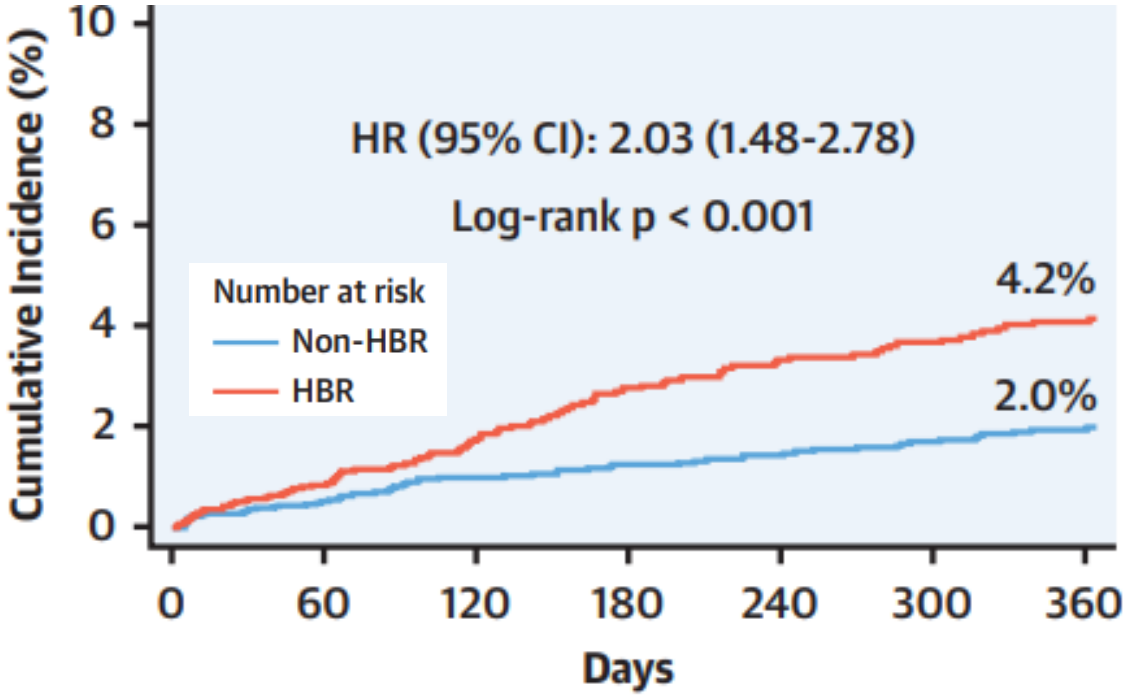
High-Bleeding Risk Patients - Who?



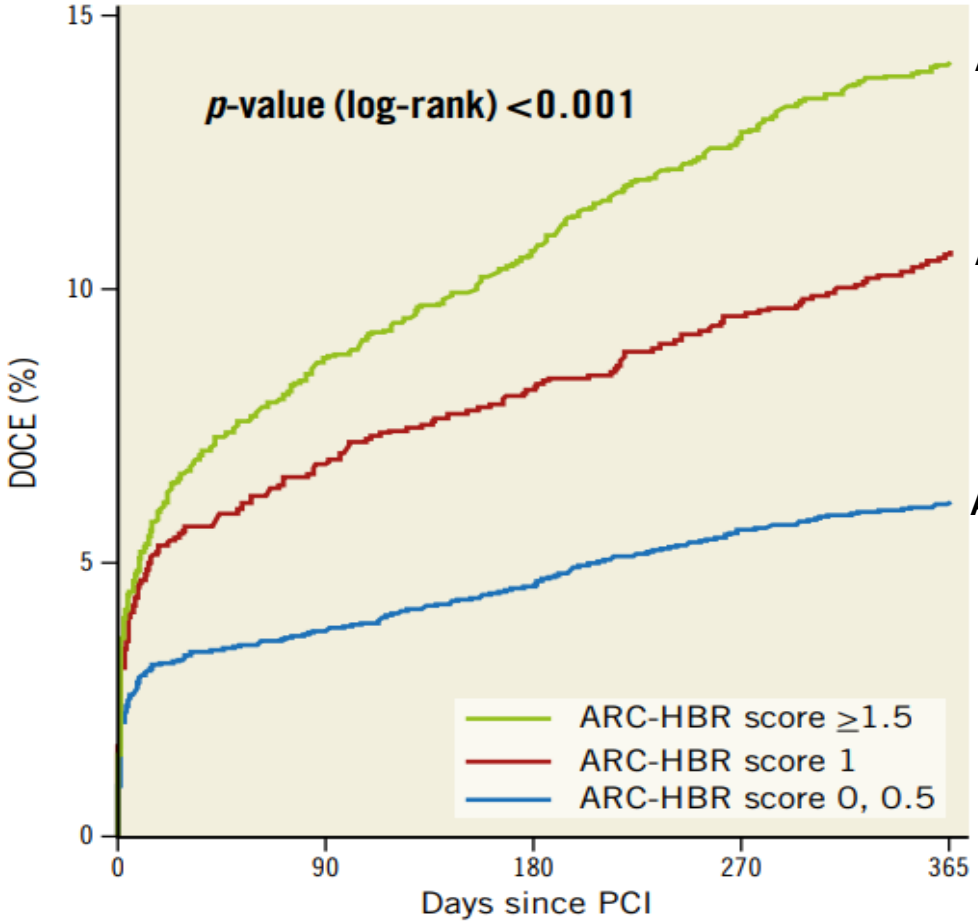
Urban P et al. Circulation. 2019;140:240–261

HBR Patients are also high-ischemic risk!

Myocardial infarction



Cardiac death, TV-MI, TLR



ARC-HBR >1.5

ARC-HBR = 1

ARC-HBR = 0, 0.5

Cao D, Mehran R, et al. J Am Coll Cardiol. 2020 Jun 2;75(21):2711-2722; Ueki Y et al. EuroIntervention. 2020

High-Bleeding Risk Patients – The Dilemma

- Contemporary DES are significantly safer than early-generation DES, which makes the use of long DAPT durations **unnecessary** for the prevention of ST during the 1st year after PCI.

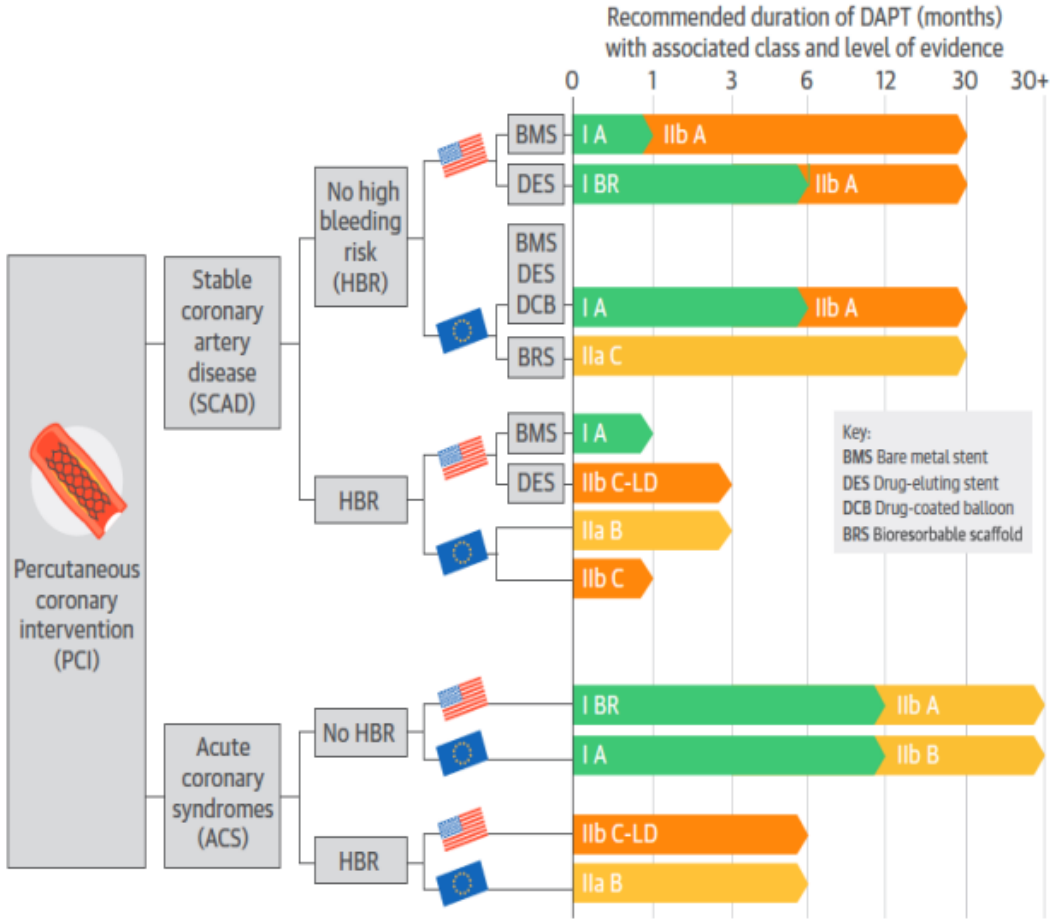
- DAPT remains of sustained utility to prevent non-DES-related events, especially in patients at high risk of thrombosis.

- The decision regarding DAPT duration requires consideration of individual patient and procedure characteristics.

- Prolonging DAPT could be detrimental in patients at high risk of bleeding, and **early discontinuation might be safe from the mere standpoint of the stent platform**.

DAPT in HBR: How Long?

ACC Vs ESC Guidelines



Weak evidence in HBR patients!

Stable CAD

No HBR	6 to 12 months
HBR	1 to 3 months

ACS

No HBR	12 to 12+ months
HBR	6 months

Capodanno D et al., J Am Coll Cardiol. 2018 Dec 11;72(23 Pt A):2915-2931.

Novel DAPT strategies in HBR patients

What are the options?

To reduce the risk of bleeding further in HBR patients, two strategies are of current investigational interest:

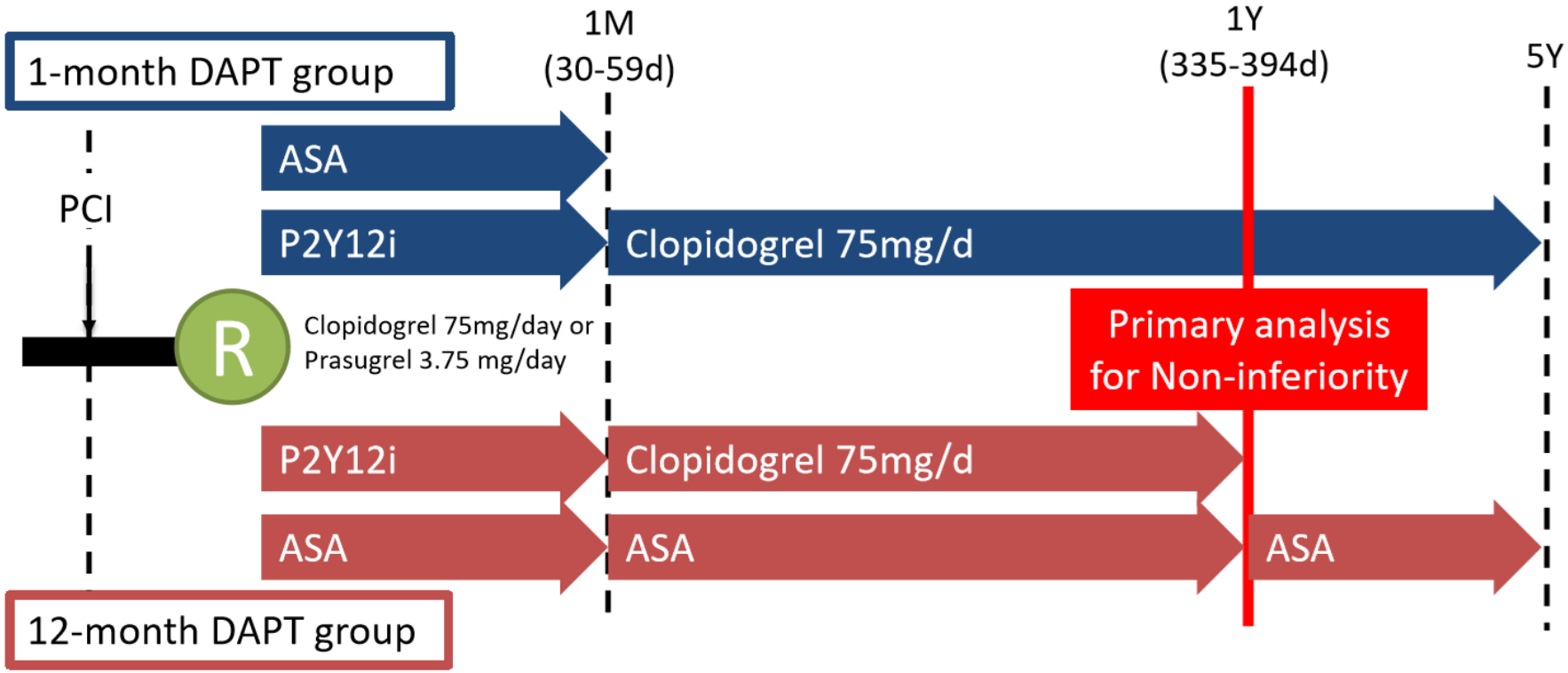
1. **<u>Shortening DAPT</u>:** by dropping the $P2Y_{12}$ inhibitor or aspirin
   (Evaluated in **<u>HBR</u>** patients).

2. **<u>Modulating DAPT</u>:** by means of **de-escalation** of drug types and doses
   (Evaluated in **<u>all</u>** patients).

Recent studies on SHORTENING DAPT in HBR patients

1-Month DAPT Followed by Clopidogrel vs 12-Month DAPT on CV and Bleeding Events in Patients Undergoing PCI

The STOPDAPT-2 Trial



Presented by Dr Hirotoshi Watanabe at ACC 2019

STOPDAPT-2 Trial:

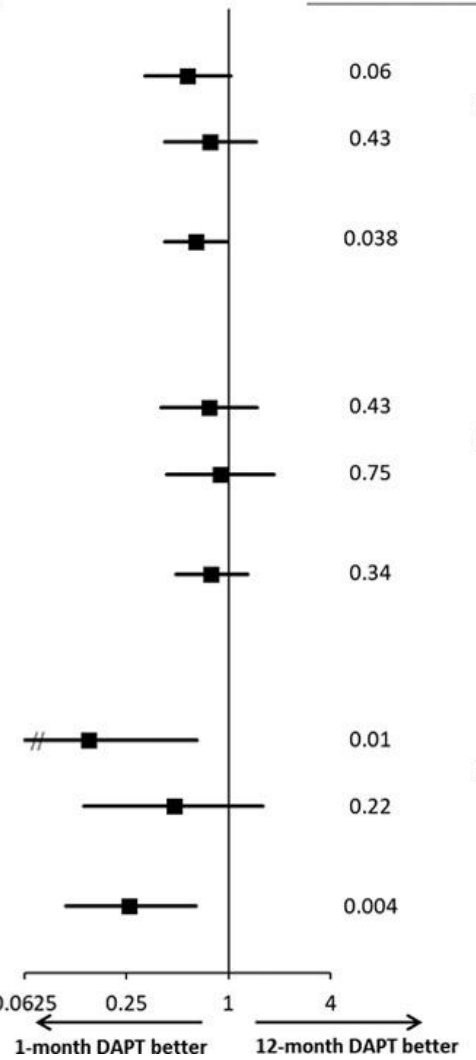
HBR Sub-study

NACE

MACE

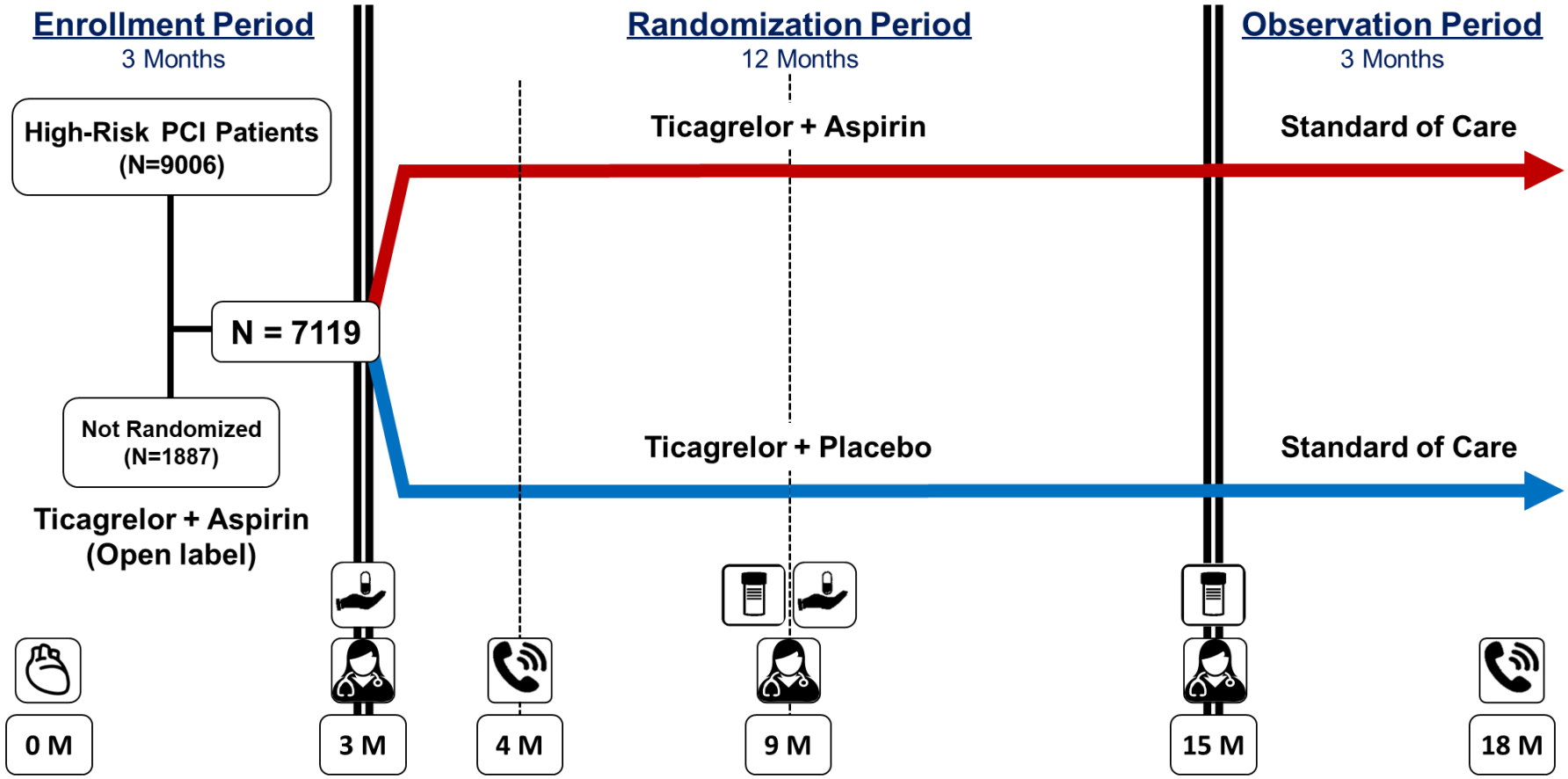
TIMI major or minor Bleeding

	Cumulative 1-year incidence (N of patients with event/ N of patients)					
	1-month DAPT (N=1500)	12-month DAPT (N=1509)	Absolute difference (95%CI)	Hazard Ratio (95%CI)	P value	P interaction
Primary Endpoint						
HBR	3.48% (17/496)	5.98% (33/558)	-2.50% (-5.06% to 0.06%)	0.57 (0.32-1.03)	0.06	0.48
Non-HBR	1.81% (18/1004)	2.36% (22/951)	-0.55% (-1.83% to 0.73%)	0.78 (0.42-1.45)	0.43	
Overall	2.36% (35/1500)	3.70% (55/1509)	-1.34% (-2.57% to -0.11%)	0.64 (0.42-0.98)	0.038	
Major Secondary Cardiovascular Endpoint						
HBR	3.07% (15/496)	4.03% (22/558)	-0.96% (-3.21% to 1.29%)	0.77 (0.40-1.48)	0.43	0.77
Non-HBR	1.41% (14/1004)	1.61% (15/951)	-0.20% (-1.28% to 0.88%)	0.89 (0.43-1.84)	0.75	
Overall	1.96% (29/1500)	2.51% (37/1509)	-0.55% (-1.62% to 0.52%)	0.79 (0.49-1.29)	0.34	
Major Secondary Bleeding Endpoint						
HBR	0.41% (2/496)	2.71% (15/558)	-2.30% (-3.77% to -0.83%)	0.15 (0.03-0.65)	0.01	0.22
Non-HBR	0.40% (4/1004)	0.85% (8/951)	-0.45% (-1.16% to 0.26%)	0.48 (0.14-1.58)	0.22	
Overall	0.41% (6/1500)	1.54% (23/1509)	-1.13% (-1.84% to -0.42%)	0.26 (0.11-0.64)	0.004	



Watanabe H et al. Circulation. 2019;140:1957–1959

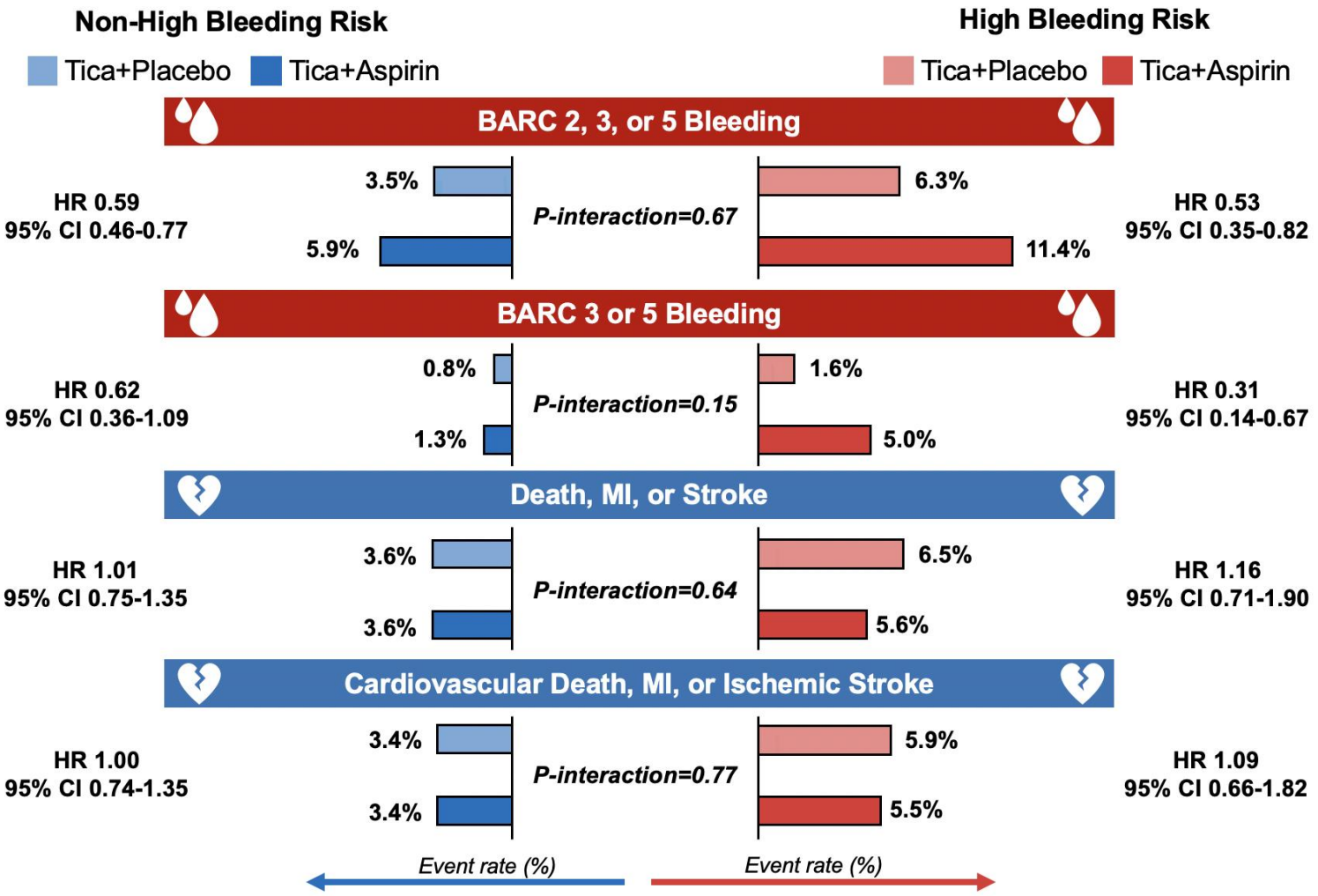
TWILIGHT Trial – Ticagrelor Monotherapy After PCI



Presented by Dr Mehran at TCT 2019

TWILIGHT Trial:

HBR Sub-study



Escaned J et al. Eur Heart J. 2021 Dec 1;42(45):4624-4634.

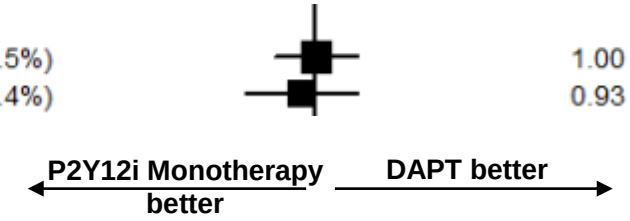
P2Y12 Inhibitor Monotherapy After Short DAPT

An IPD meta-analysis of 24,096 patients

Trials included: **DACAB, GLASSY, SMART-CHOICE, STOPDAPT-2, TICO, and TWILIGHT**

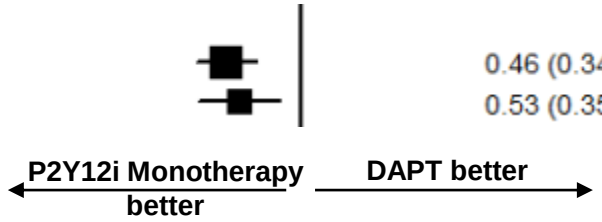
All-cause death, MI, or stroke

	P2Y12i monotherapy (N=10766)	DAPT (N=11195)	HR (95% CI)	p value for interaction
High bleeding risk				
PRECISE DAPT <25	177/8370 (2.4%)	183/8714 (2.5%)	1.00 (0.81-1.23)	0.570
PRECISE DAPT ≥ 25	94/1769 (5.6%)	108/1870 (6.4%)	0.93 (0.70-1.23)	



BARC 3 or 5 bleeding

High bleeding risk				
PRECISE DAPT < 25	59/9031 (0.7%)	128/9059 (1.6%)	0.46 (0.34-0.63)	0.730
PRECISE DAPT ≥ 25	34/1941 (1.9%)	66/1987 (3.5%)	0.53 (0.35-0.80)	



Valgimigli M and Mehran R et.al., BMJ, 2021.

DAPT after PCI in Patients at HBR

MASTER-DAPT Trial

Screened Population: **HBR pts, treated exclusively with Ultimaster stent, with no restriction based on clinical presentation (12% STEMI) or PCI complexity**

30 (+14) Days after PCI

Free from cardiac and cerebral ischemic events
and active bleeding
No further revascularization planned

Sx: Site
Need for oral anticoagulation
Prior MI within 12 months

Abbreviated DAPT

Immediate DAPT discontinuation

followed by SAPT for 11 months
or 5 months if OAC is indicated

Standard DAPT

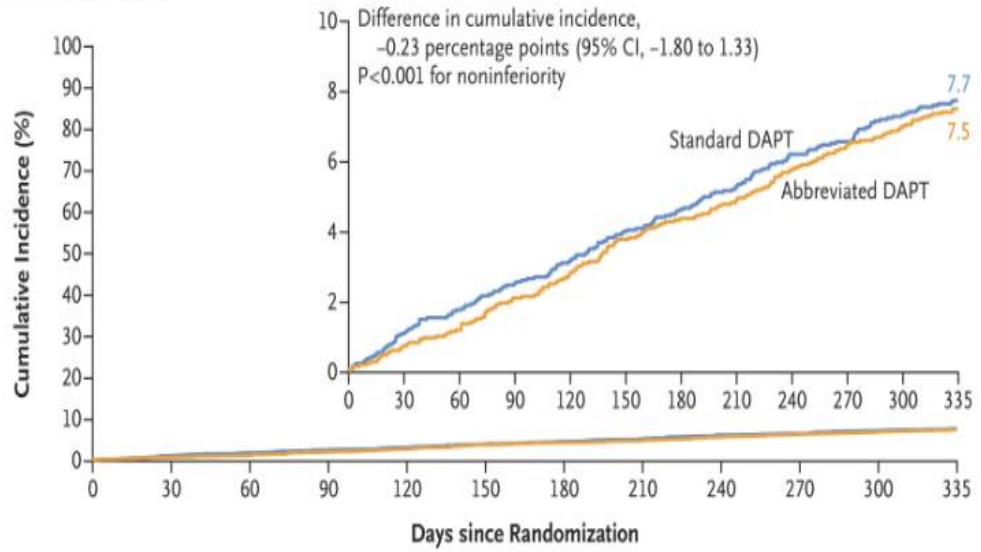
DAPT for ≥ 2 or 5 months in pts with or without OAC indication, respectively

followed by SAPT up to 11 months

Presented by Dr Valgimigli at ESC 2021

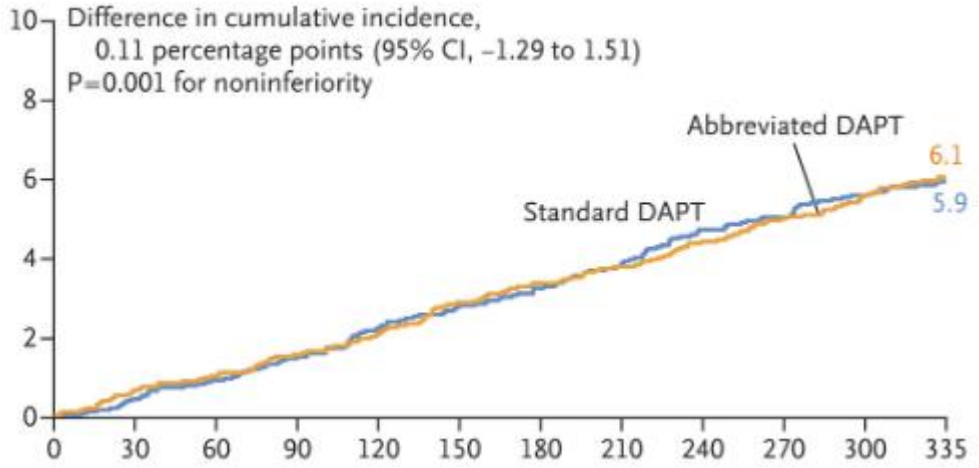
DAPT after PCI in Patients at HBR
MASTER-DAPT Trial

Primary Outcome
Death, MI, stroke, or major bleeding

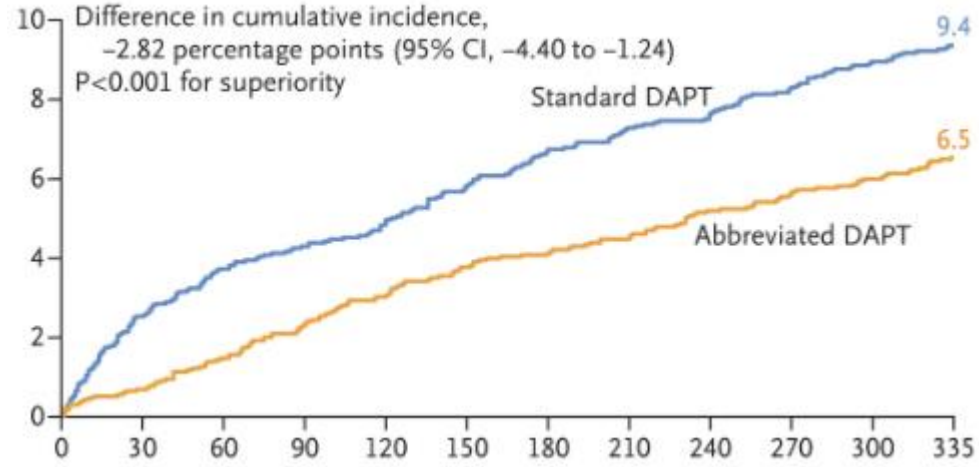


No. at Risk												
Standard DAPT	2230	2203	2188	2169	2155	2137	2118	2102	2081	2068	2052	2041
Abbreviated DAPT	2204	2184	2173	2153	2138	2144	2101	2091	2070	2056	2044	2027

MACCE



Major Bleeding



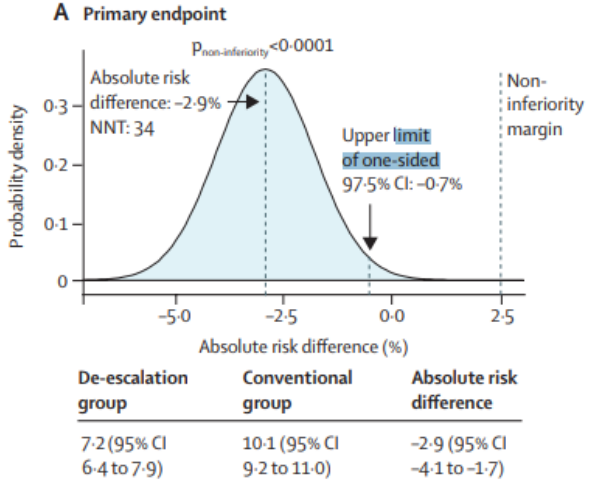
Valgimigli M et al., NEJM, 2021

Recent studies on **MODULATING** DAPT in HBR patients *(Most likely beneficial)*

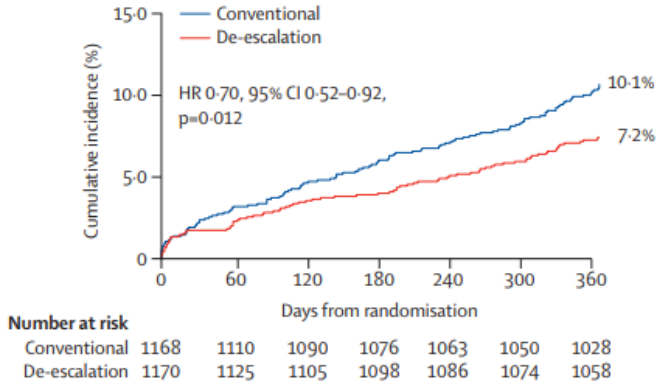
Prasugrel-based de-escalation of DAPT after PCI in patients with ACS - HOST-REDUCE-POLYTECH-ACS

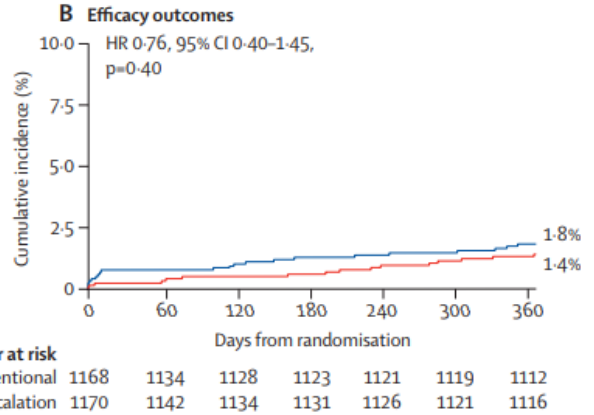
2338 patients were randomly assigned to the de-escalation group (n=1170) or the conventional group (n=1168)

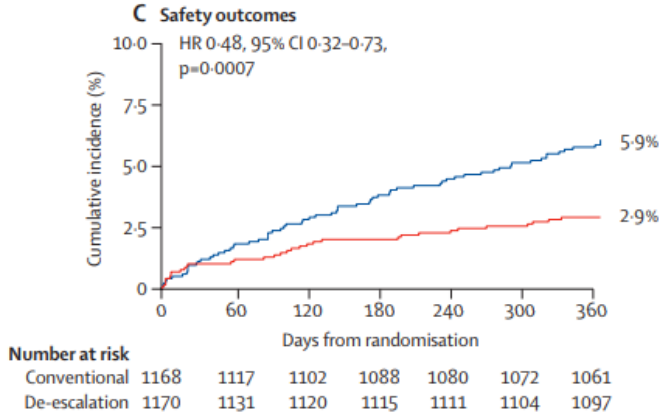
In East Asian ACS patients undergoing PCI, a prasugrel-based dose de-escalation strategy (from 10 to 5 mg) from 1 month after PCI reduced the risk of net clinical outcomes up to 1 year, mainly driven by a reduction in bleeding without an increase in ischaemia.



De-escalation group	Conventional group	Absolute risk difference
7·2 (95% CI 6·4 to 7·9)	10·1 (95% CI 9·2 to 11·0)	−2·9 (95% CI −4·1 to −1·7)

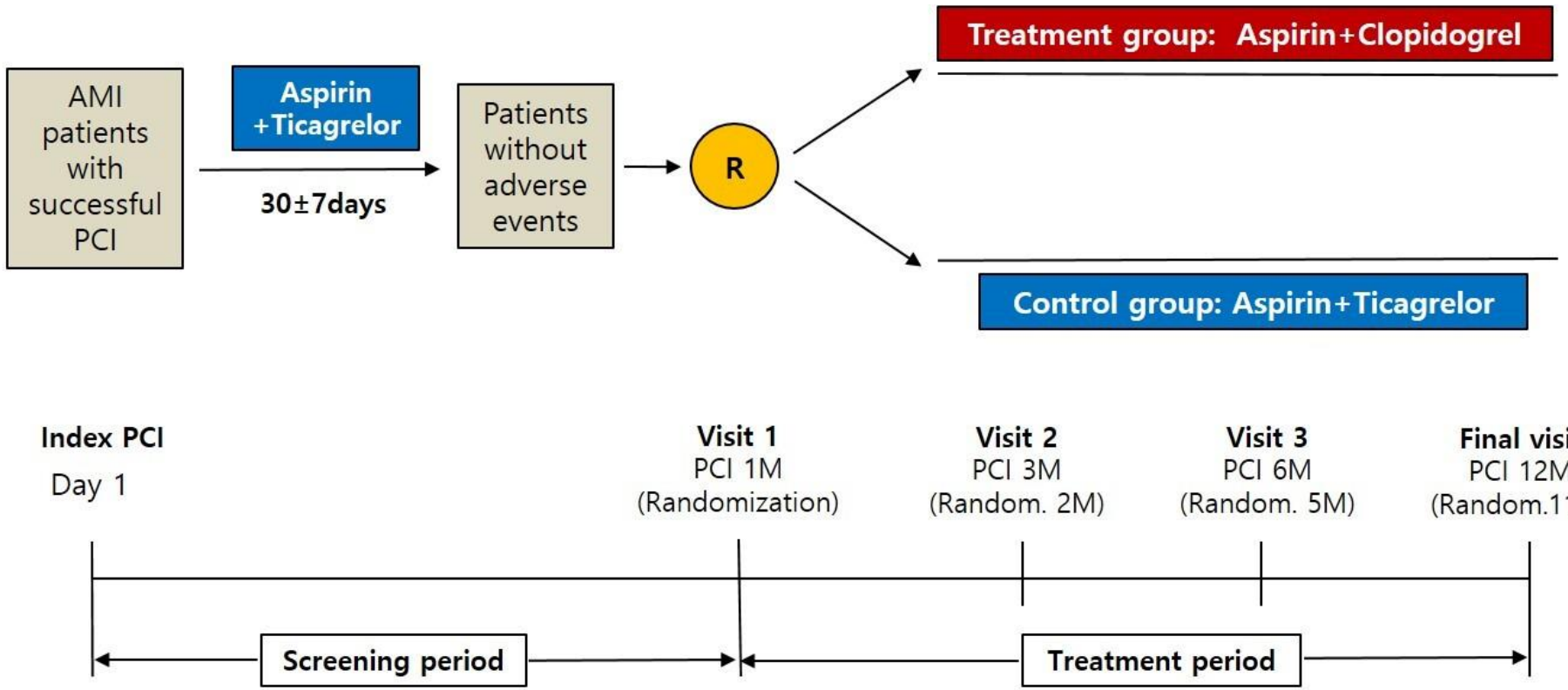






Kim HS et al. Lancet 2020; 396: 1079–89

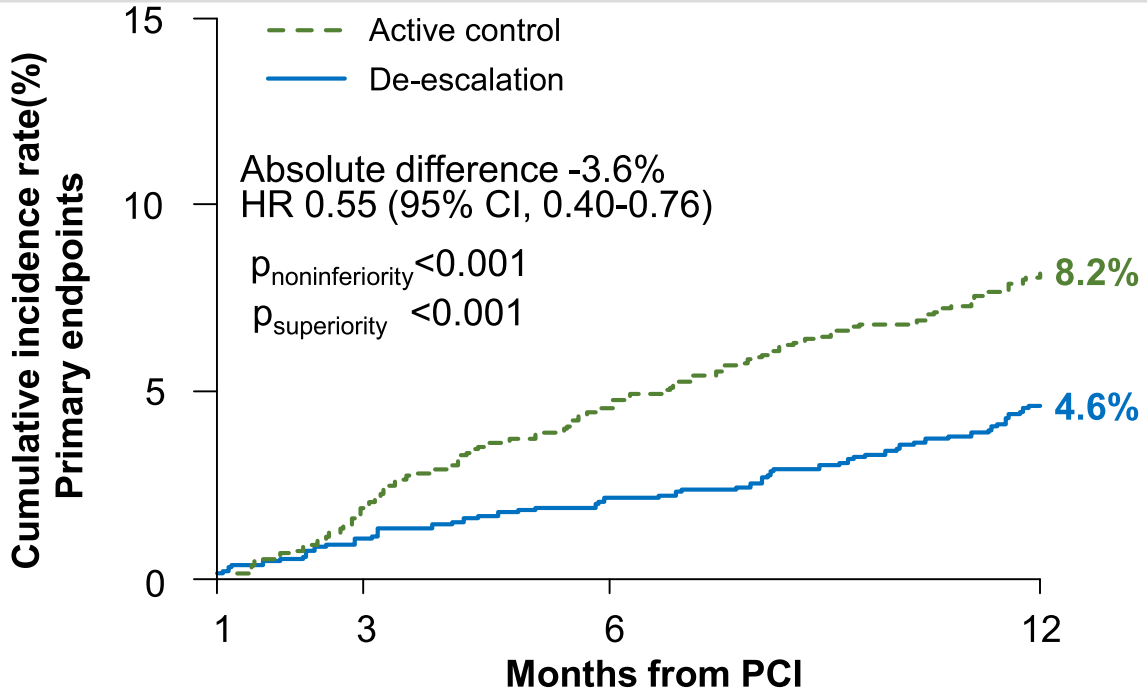
Ticagrelor vs. Clopidogrel in Stabilized Patients with AMI: TALOS-AMI Trial



Presented By Dr Kiyuk Chang at ACC 2021

Ticagrelor vs. Clopidogrel in Stabilized Patients with AMI: TALOS-AMI Trial

Composite of cardiovascular death, MI, stroke and **BARC bleeding (type 2,3, or 5)**



In AMI patients who had no major adverse events during the first month after an index PCI, **a uniform, unguided de-escalation DAPT strategy switching from ticagrelor to clopidogrel was superior to the ticagrelor-based continuing DAPT strategy in terms of net clinical benefit, with a significant decrease in bleeding risk and no increase in ischemic risk.**

Presented By Dr Kiyuk Chang at ACC 2021

De-Escalation Strategies: A Meta-Analysis

Results

11 RCTs and 3 observational studies with data for 20 743 patients.

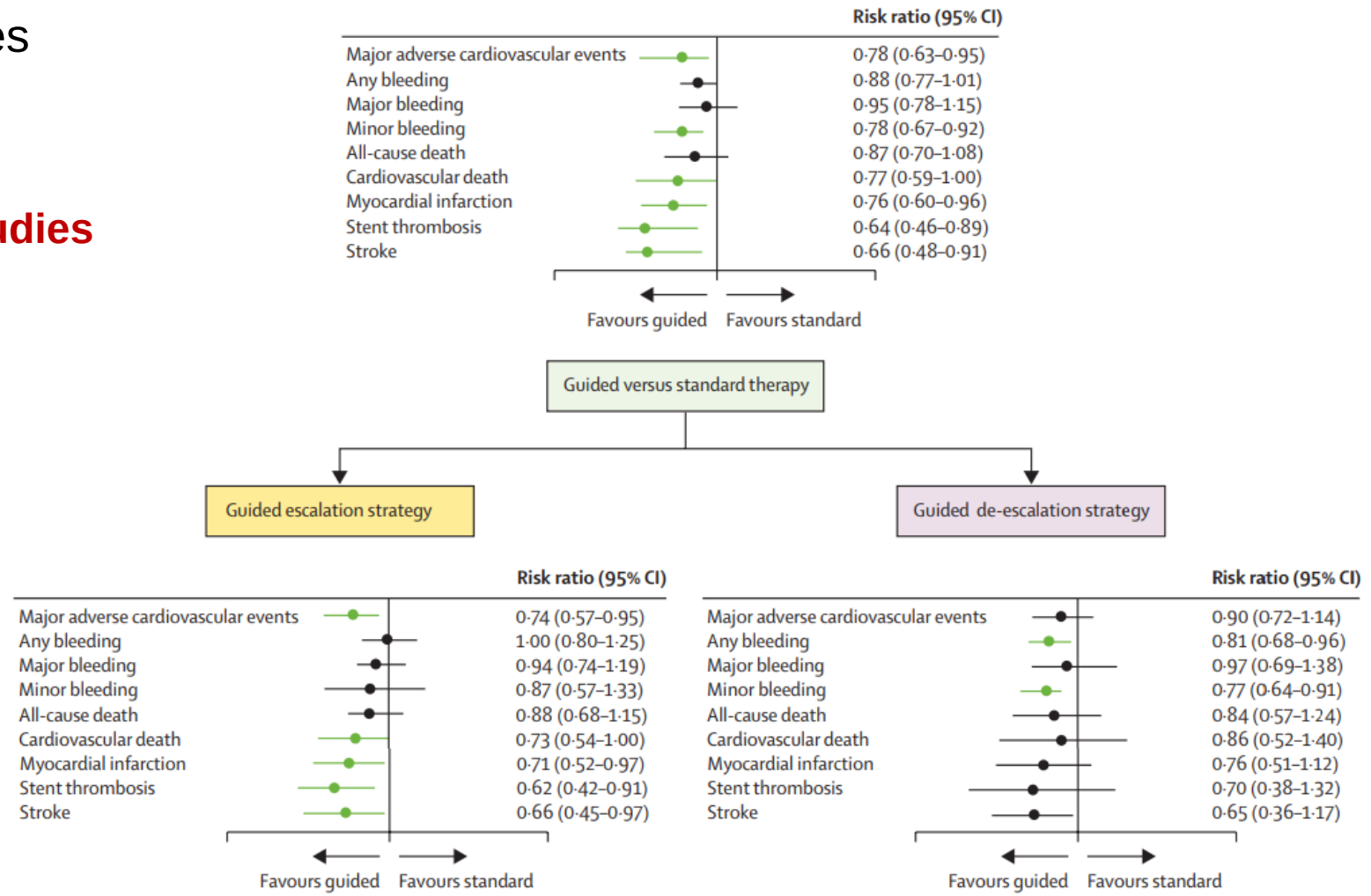
11 RCTs

POPular Genetics[19]
TAILOR-PCI[20]
ARCTIC[21]
ANTARCTIC[22]
TROPICAL-ACS[23]
PHARMCLO[24]
IAC-PCI[29]
Zhu et al[30]
PATH-PCI[31]
Tuteja et al[32]
Hazarbasanov et al[33]

3 Observational Studies

Shen et al[34]
Sánchez-Ramos et al[35]
Lee et al[36]

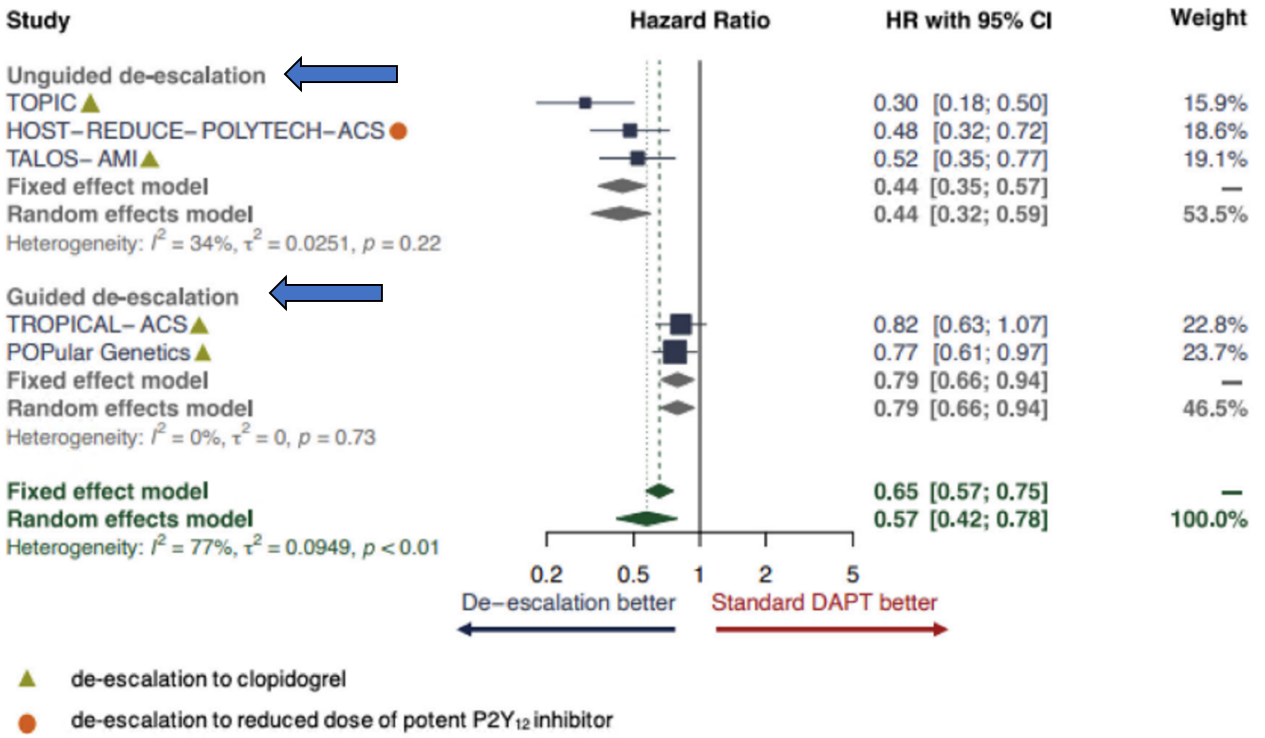
TALOS AMI not included!



Galli M et al., The Lancet. 2021

Guided and Unguided De-Escalation from Potent P2Y12 Inhibitors Among Patients with ACS: a Meta-Analysis

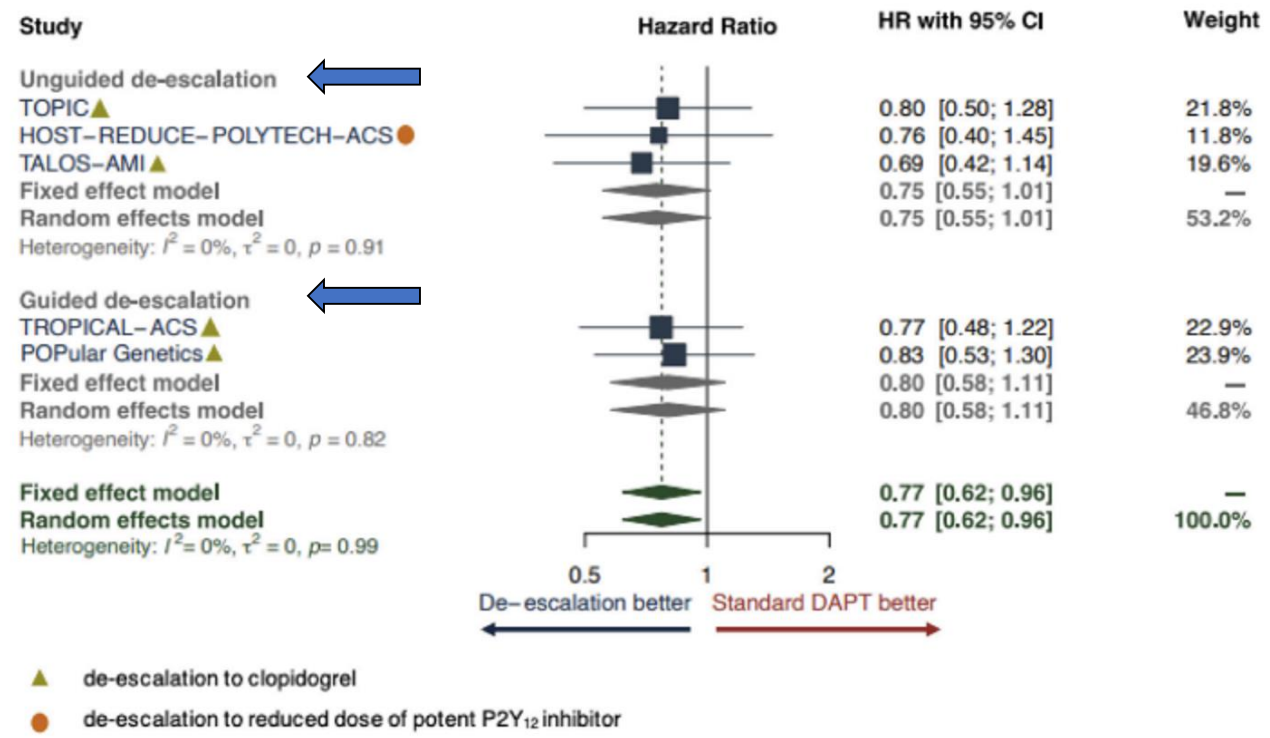
BARC 2-5 Bleeding



▲ de-escalation to clopidogrel

● de-escalation to reduced dose of potent $P2Y_{12}$ inhibitor

MACE



▲ de-escalation to clopidogrel

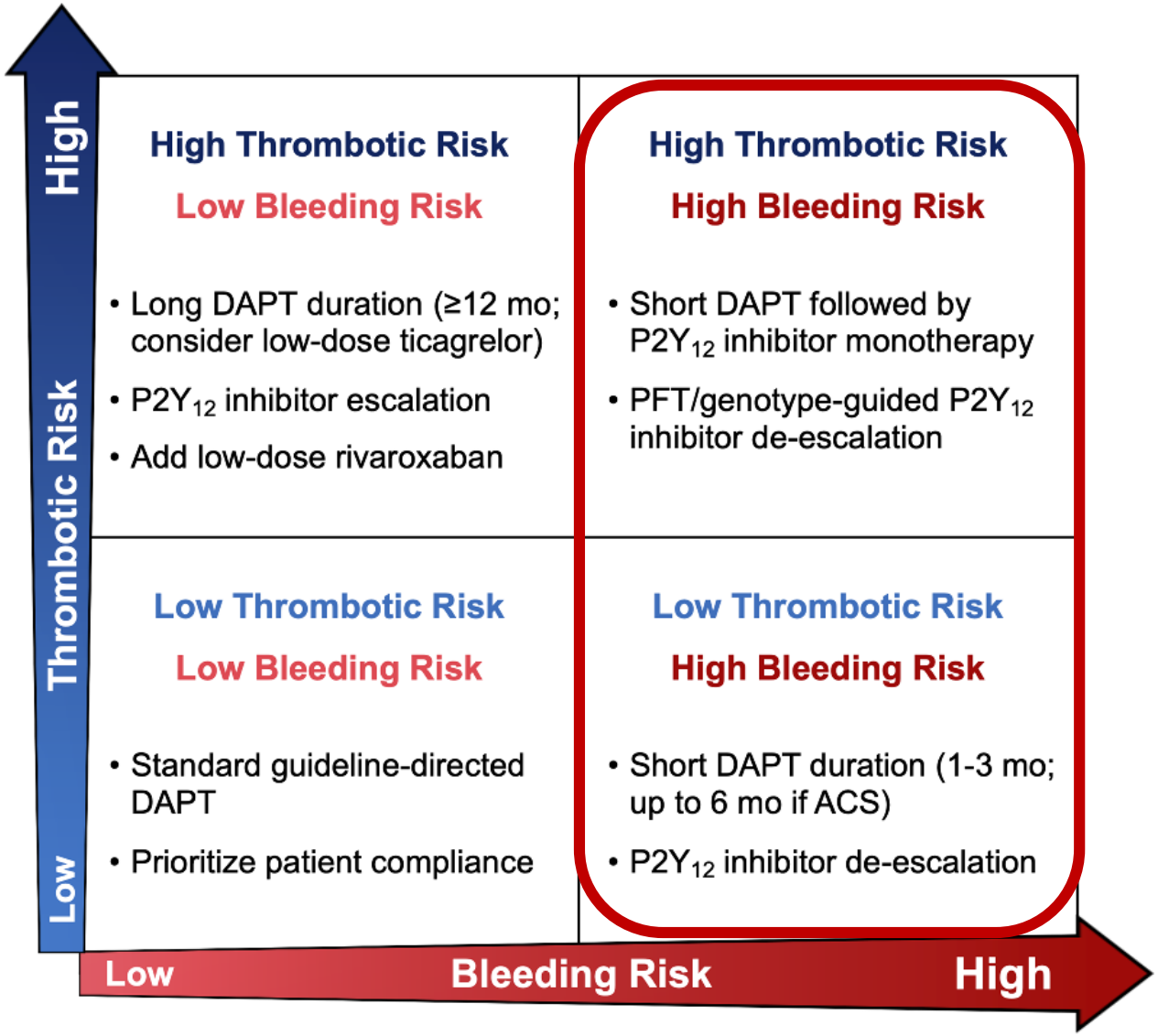
● de-escalation to reduced dose of potent $P2Y_{12}$ inhibitor

TALOS AMI included!

Tavenier AH, Dangas G et al., EHJ CVP, 2021

Take-Home Messages

No single DAPT recommendation applies to every patient.



Cao D et al., Eur Heart J. 2020 Dec 26;ehaa824.